Attorney's Docket No. B252 1280US (63141 0168.3) PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.:	10/032,657	Confirmation No.: 6168
Applicant(s):	Banerjee *et al.*	
Filed:	December 28, 2001	
Art Unit:	1641	
Examiner:	Pensee T. Do	
Title:	MULTIANALYTE MOLCULAR ANALYSIS USING APPLICATION-SPECIFIC RANDOM PARTICLE ARRAYS	

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APPEAL BRIEF UNDER 37 CFR § 41.37

This Appeal Brief is filed pursuant to the "Notice of Appeal to the Board of Patent Appeals and Interferences" filed December 8, 2010, which was filed in response to the Office Action dated June 9, 2010.

1. Real Party in Interest.

The real party in interest in this appeal is BioArray Solutions, Ltd., the assignee of the above-referenced patent application, which is a subsidiary of ImmuCor, Inc.

2. Statement of Related Cases.

There are no related appeals, continuing applications, or interferences involving this application or its subject matter.

3. Status of Claims.

Claims 18-22 are pending and all stand rejected as unpatentable over a combination of prior art references as set forth in greater detail below. All rejections of record are appealed herein. Accordingly, the rejections of all of claims 18-22 are appealed herein.

4. Status of Amendments.

All claim amendments presented during prosecution have been entered and are set forth in the clean copy of the pending claims appended to the brief. A response was filed on December 8, 2010 in response to the final rejection; however, no after-final amendments to the claims were submitted therein. Claim 18 was amended twice during prosecution. Claim 21 was amended once during prosecution. Claims 19, 20, and 22 were not amended during prosecution.

5. **Summary of Claimed Subject Matter.**

The present invention is directed to a method of multiplex analysis of analytes in solution. Independent claim 18 is the sole pending independent claim. Claim 18 recites a method comprising the steps of providing a plurality of magnetically polarizable microparticles wherein the different types bear optically distinguishable signatures and display different capture moieities on their surfaces, suspending the microparticles in a solution containing or suspected to contain analytes of interest, using a magnetic field to assemble the microparticles into a planar array, and imaging the signatures associated with the microparticles to determine which analytes are bound by which capture moieties.

The step of providing a plurality of magnetic particles is described, for example, at page 21, beginning at line 11. Magnetically polarizable microparticles of two or more types can be encoded with a chemically or physically distinguishable characteristic (*e.g.*, an optically distinguishable signature) (*see* page 12, lines 8-20 and page 21, lines 17-18). One exemplary process for the preparation of such microparticles is described at page 21, line 25 through page 23, line 18. The microparticles can display different capture moieties on their surfaces (*see, e.g.*, page 12, line 22 through page 13, line 7 and page 23, line 20 through page 24, line 20). Example 16b, beginning on page 49, line 9, provides an

example of the incorporation of capture moieties (here, a protein) on the surfaces of microparticles. These microparticles thus can form a plurality of magnetically polarizable microparticles wherein different types bear an optically distinguishable signature and the different types display different capture moieties on their surfaces (*see, e.g.,* page 27, lines 10-20).

The microparticles are suspended in a solution containing, or suspected to contain analytes (*see, e.g.,* page 15, line 7 through page 17, line 3). An optical signature can be generated following the capture of analytes from the solution (*see, e.g.,* page 17, line 18 through page 18, line 14).

The microparticles can be assembled into a planar array on a designated area of a substrate using a magnetic field (*see, e.g.,* page 21, lines 21through 23; page 25, line 27 through page 26, line 18; and page 32, line 13 through page 33, line 14). Either "coils or magnets" can be used for this purpose (*see, e.g.*, page 52, lines 14 through 20). The Examples demonstrate certain embodiments of magnetic assembly of magnetic microparticles (*see, e.g.*, Example 3 at page 35, line 19 through page 36, line 4; and Example 18, at page 52, line 11 through 29). The specific parameters of the magnetic field recited in the claims are discussed, for example, at page 26, lines 17 and 18 ("uniform magnetic field"), and at page 26,

lines 13-15 ("As a function of increasing magnetic field strength, ordered planar assemblies of field-dependent number density ... can be formed.").

6. Grounds of Rejection to be Reviewed.

Claims 18-22 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 7,115,884 to Walt *et al.* (hereinafter "Walt") in view of U.S. Patent No. 6,013,531 to Wang (hereinafter "Wang"), and further in view of U.S. Patent No. 5,602,042 to Farber (hereinafter "Farber").

7. Argument.

In response to the Grounds of Rejection presented herein, Applicants submit that the rejections set forth in the Final Office Action of pending claims 18-22 under 35 U.S.C. § 103(a) are improper for the reasons presented below.

I. In rejecting claims 18-22 under 35 U.S.C. § 103(a) over Walt in view of Wang and further in view of Farber, the Examiner has failed to establish a *prima facie* case of obviousness, as required by MPEP 2142 because Farber does not teach or suggest the parameters of the magnetic field recited in the pending claims.

A. Standard for obviousness under 35 U.S.C. § 103(a).

Under 35 U.S.C. § 103(a),

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

To establish a *prima facie* case of obviousness, according to a test predominately used by the courts, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim elements. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

With regard to the Supreme Court's decision in *KSR Int'l. Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007), it is noted that the Court did not dismiss the usefulness of the well-established "teaching, suggestion, or motivation" test set forth above, but merely cautioned against its rigid application. The Supreme Court in *KSR* commented that the Federal Circuit ''no doubt has applied the test in accord with these principles [set forth in *KSR*] in many cases.'' *Id.* 82 USPQ2d at 1396. However, the Supreme Court also opined that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. . ." *Id.* 82 USPQ2d at 1395-96. Regardless of the precise test used, the Court, quoting *In re Kahn*, cautioned that '' '[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.' '' *Id.* 82 USPQ2d at 1396.

B. Examiner's rejection of claims 18-22.

The Examiner argues that Walt teaches a method of multiplex analysis of analytes in solution, comprising providing subpopulations of microspheres with distinct optical response signatures or different associated fluorescent dyes with capture moieties thereon, assembling the microspheres into an array and adding a

sample, illuminating the array, and decoding the array by comparison to a known analyte or a library of optical response signatures for its corresponding microsphere subpopulation type. The Examiner argues that it would have been obvious to modify the method of Walt by using fluorescent magnetic beads as markers in assays, as taught by Wang. The Examiner further argues that it would have been obvious to modify the method of Walt and Wang by applying a magnetic field to the beads to form an assembly, as taught by Farber.

In particular, with regard to the parameters of the magnetic field recited in the pending claims, the Examiner asserts that, "Farber teaches that the particles are uniformly collected against the substrate surface and therefore, the magnetic field must be uniformly distributed across the substrate in order to uniformly collect the magnetic particles" (*see* Final Official Action, page 7). The Examiner further alleges that Farber teaches the selective activation/deactivation of a distributed array of magnets, and that the magnetic field of the individual magnets/coils is varied and can therefore adjust the inter-particle spacing.

C. Differences between claimed invention and cited art.

Independent claim 18 recites, in pertinent part, that the method requires using a magnetic field to assemble the microparticles "in a planar array on a designated section of a substrate, where said magnetic field is generated by coils or magnets,

and is uniformly distributed over the surface of the substrate, and wherein the spacing between particles within the array can be varied by varying the strength of the magnetic field." Applicants respectfully submit that Farber does not teach the magnetic assembly step recited by claim 18. Specifically, Farber does not teach or suggest the particular magnetic field characteristics recited in the claims.

First, with regard to the recitation in claim 18 of a magnetic field that is "uniformly distributed" over the surface of the substrate, Farber does not teach such a uniformly distributed field. In general, Farber teaches a system wherein a "spatially distributed array of magnetic elements ... allows the strength of the magnetic field to be varied over the area of the surface" (*see* column 7, lines 38-42 of Farber). The magnetic elements of Farber are posts connected to a magnetic element, wherein the posts are arranged against a surface to produce a magnetic field with a selected spatial distribution. For example, see Figures 1 and 2 of Farber (in particular, element **30** in these figures, which represents the magnetic posts). Farber notes that the magnetic field strength of these posts is controlled, allowing these posts to be separately activatable to give a magnetic system that is "time varying and spatially varying under the control of the control system" (*see* column 7, lines 46-47). The system taught by Farber does not comprise a magnetic field that is uniformly distributed over the surface of a substrate, as required by

claim 18 of the present application.

The Examiner asserts that Farber "teaches that the particles are uniformly collected against the substrate surface and therefore, the magnetic field must be uniformly distributed across the substrate in order to uniformly collect the magnetic particles (*see* Final Official Action, page 7). However, the teaching of Farber is focused on the concept of a "spatially varying magnetic field," which is used to "control the spatial distribution of the cells collected against the plate" (see column 3, lines 64-66 of Farber). The magnetic field described in Farber is varied spatially and is thus inherently non-uniform.

There is no reference in Farber to a "uniform" distribution of a magnetic field. Further, there is no teaching or suggestion that the "more uniform spatial distribution" of particles disclosed in Farber and pointed to by the Examiner requires a uniform magnetic field. In fact, Farber specifically states that the embodiment relied upon by the Examiner (column 3, lines 64-66) utilizes a spatially varying magnetic field.

This characteristic is further illustrated in Figure 5 of Farber. Specifically, in this embodiment, a magnet with one post at the periphery of the magnet is rotated by spinning the magnet body about a bearing. The magnet selectively rotates relative to the plate and spatially varies the induced magnetic field within the fluid

as a function of rotation rate, and therefore time (*see* column 12, line 60 through column 13, line 4).

Farber states, with regard to this configuration (for achieving more uniform spatial distribution) that the rotating disk is a means for "spatially varying the magnetic field" (*see* column 4, lines 5-7 of Farber). Thus, although Farber refers to a "more uniform" distribution of particles that may be achieved by this method, this distribution is not achieved with a "uniform" magnetic field as required by the presently pending claims. Rather, the spatial distribution is specifically described as being achieved by "spatially varying" the magnetic field. As such, the Examiner's conclusion that the magnetic field "must be uniformly distributed" because Farber teaches that particles are "uniformly" collected against the surface is in error. Claim 18 of the present application recites a uniform magnetic field, which is not taught or suggested by Farber.

Second, with regard to the recitation in claim 18 that spacing between particles may be varied by varying the strength of the magnetic field, Farber does not teach or suggest such a result. The Examiner alleges that Farber teaches the selective activation/deactivation of a distributed array of magnets, and that the magnetic field of the individual magnets/coils is varied and can therefore adjust the inter-particle spacing. The arrangement of posts extending from a magnet to a

plate collection surface to vary the strength of the field across the collection surface taught by Farber (*see* column 7, lines 26-30) is simply not taught to be capable of achieving this goal.

The reference in Farber to a distributed array of magnets that can be selectively activated and deactivated to spatially vary the magnetic field is not analogous to the system claimed herein, with "spacing between particles" within the same array that can be "varied by varying the strength of the magnetic field." Farber does not discuss the spacing between particles. It is understood based on Farber that the system therein provides for control over inter-particle spacing only through selective activation of certain posts (**30**) extending from the magnetic element. Thus, groups of particles would accumulate at activated posts (and not at the deactivated posts). The spacing within a particular group of particles on the plate surface at a given post is not discussed in Farber. Farber does not teach or suggest that there is any means by which this spacing could be controlled. The only method of control of particle spacing possible based on the teaching of Farber is general control over the location of particle assemblies on the surface of the substrate by selective activation/deactivation of magnetic posts contacting the substrate, and not any control over the particles within one of those particle assemblies. This is in clear contrast to the presently claimed method, wherein

spacing between particles within an array is specifically varied by varying the strength of the magnetic field.

Because Farber does not teach or suggest using a magnetic field to assemble microparticles in a planar array, wherein the magnetic field is uniformly distributed over the surface of the substrate, and wherein the spacing between particles within the array can be varied by varying the strength of the magnetic field, this rejection is in error. For at least these reasons, Walt in view of Wang and further in view of Farber, fails to teach or suggest all of the required claim elements. Accordingly, it is requested that the Board of Patent Appeals and Interferences reverse the rejection of claims 18-22 and remand the case to the Examiner for allowance of all claims pending herein.

8. Claims Appendix.

An appendix containing a copy of the claims involved in the appeal is attached.

9. Evidence Appendix

No evidence has been submitted to the Examiner or relied upon by the Applicants.

10. Related Proceedings Appendix

There are no decisions by a court or the Board in related proceedings.

11. Conclusion

In summary, Walt in view of Wang and further in view of Farber does not teach or suggest the embodiments recited in Claim 18 and the claims depending therefrom. In light of the foregoing, Applicant submits that the pending claims are not obvious over the art of record, and Applicant submits that a correct evaluation considering the evidence as a whole in its proper context and meaning supports Applicant's argument for patentability. Accordingly, Applicant respectfully requests a determination by the Board that the pending claims are allowable over the cited art and an order withdrawing the pending rejections.

Dated: March 7, 2011

Respectfully submitted,

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CLAIMS APPENDIX

Claims Appendix

1.-17. (Canceled)

18. (Previously presented) A method of multiplex analysis of analytes in a solution, comprising:

providing a plurality of magnetically polarizable microparticles of two or more types wherein different types bear an optically distinguishable signature, and the different types display different capture moieties on their surfaces capable of binding to different analytes;

suspending the microparticles in a first solution containing, or suspected to contain, analytes of interest, under conditions permitting the capture of analytes by the capture moieties, and wherein an optical signal is generated following such capture;

using a magnetic field to assemble the microparticles in a planar array on a designated section of a substrate, where said magnetic field is generated by coils or magnets, and is uniformly distributed over the surface of the substrate, and wherein the spacing between particles within the array can be varied by varying the strength of the magnetic field; and

imaging the optically distinguishable signatures associated with the microparticles and the optical signals, and correlating the optical signals with microparticles having particular optically distinguishable signatures to determine which analytes are bound by which capture moieties.

19. (Previously presented) The method of claim 18 wherein the optical signals arise as a result of the binding of an analyte by a capture moiety.

20. (Previously presented) The method of claim 19 wherein the optical signal indicates the transformation of the capture moiety mediated by the binding of the analyte.

21. (Previously presented) The method of claim 18 wherein the first solution is removed and replaced with a second solution prior to imaging the optically distinguishable signatures associated with the microparticles and the optical signals.

22. (Previously presented) The method of claim 18 wherein array assembly is initiated at a preselected time by actuating a magnetic field.

EVIDENCE APPENDIX

Evidence Appendix

None

RELATED PROCEEDINGS APPENDIX

Related Proceedings Appendix

None